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Cohort Study Among Workers Exposed to Benzene in China: II. Exposure Assessment

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This report describes a retrospective exposure assessment method used in a follow-up mortality study of workers exposed to benzene. The approach quantified historical exposure to benzene in a multi-industry, multicenter cohort, involving 672 factories in 12 cities in China. Historical exposure data were collected to obtain exposure information related to 1,427 work units (departments) and 3,179 unique job titles from benzene-producing or -using factories in which written records and other data sources were evaluated. The basic unit for exposure assessment was a factory/work unit/job title combination which was considered separately during each of seven calendar-year time periods between 1949 and 1987 for a total of 18,435 exposure assignments. Historical information collected to estimate exposure included benzene monitoring data; lists of raw materials and factory products, and the percentage of benzene in each; the total amount and dates of use of benzene or benzene-containing materials; use of engineering controls and personal protective equipment; and other available exposure information. Overall, 38% (ranging from 3% for the earliest periods to 67% for the last period) of the estimates were based primarily on benzene monitoring data. In the absence of job-specific benzene monitoring data for a given calendar period, measurement results or exposure estimates for similar jobs and/or other calendar periods were used in conjunction with other exposure information to derive estimates. Estimated exposure levels are presented by industries and occupations. The highest average exposures during 1949–1987 were observed for the rubber and plastic industry (30.7 ppm), and for rubber glue applicators (52.6 ppm).

Key words: exposure estimates, benzene exposure, exposure assessment method, reconstruction of historical exposure

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INTRODUCTION

In studying the relationship between occupational exposure and cancer, it is often necessary to reconstruct historical occupational exposures. Among the numerous problems complicating such efforts, is the limited availability of historical occupational exposure information for certain specific job titles and/or time periods. To address the problem of limited exposure information, industrial hygienists recently have begun developing new approaches for quantitative assessment of exposure in both retrospective cohort and case-control occupational epidemiologic studies.

This report describes the exposure assessment method used to estimate historical exposure to benzene in a retrospective cohort study of 75,008 workers in 12 cities in the People's Republic of China, and to assign exposure estimates for 18,435 factory/work unit/job title/calendar-year combinations in 672 factories using or producing benzene. Although a variety of methods have been used in retrospective assessment of exposure to benzene [Ott et al., 1978; White et al., 1982; Bond et al., 1986; Aksoy et al., 1987; Rinsky et al., 1987; Yin et al., 1987; Swaen and Meijers, 1989; Brugnone et al., 1989; Hein et al., 1989; Steineck et al., 1990; Paustenbach et al., 1992], our approach was the most comprehensive effort to date to quantify historical exposure to benzene in a large multi-industry, multicenter cohort study.

METHODS

History of Occupational Exposure to Benzene in China

Benzene has had wide industrial use in China. Until the early 1970s, pure benzene was commonly used as a solvent in various paints, varnishes, glues, coatings, and other products. During 1972–1975, the occupational health hazards associated with benzene exposure (particularly leukemia, aplastic anemia, and chronic benzene poisoning) received increasing attention, and control measures were initiated. Ventilation was improved, and other solvents, such as xylene and toluene, were substituted for pure benzene. These changes generally resulted in dramatic decreases in work place air levels of benzene, as documented by routine air monitoring [Yin et al., 1987].

Air monitoring for benzene exposure was first employed in Chinese factories in the 1960s. Initially, the colorimetric method which involves nitration followed by reaction with ketones [Dolin, 1943] was used, until gas chromatography became available in 1972. In 1975, a nationwide uniform protocol for collection (by direct sampling with an air-tight syringe) and gas chromatographic analysis (by direct injection of collected gas) of benzene in air samples was developed by investigators at the Institute of Occupational Medicine of the Chinese Academy of Preventive Medicine (IOM-CAPM) [Yin et al., 1987].

Overview of the Study

The general characteristics of the cohort are described in the accompanying Part I of this series [Yin et al., 1994]. The exposure assessment part of this study was designed to provide historical estimates of benzene exposure since 1949 for 75,008 workers employed for at least 1 day during 1972–1987 in 672 benzene-exposed factories in 83 different types of industries. Altogether, exposure estimates were made for 18,435 factory/work unit (department)/job title/calendar-year time period

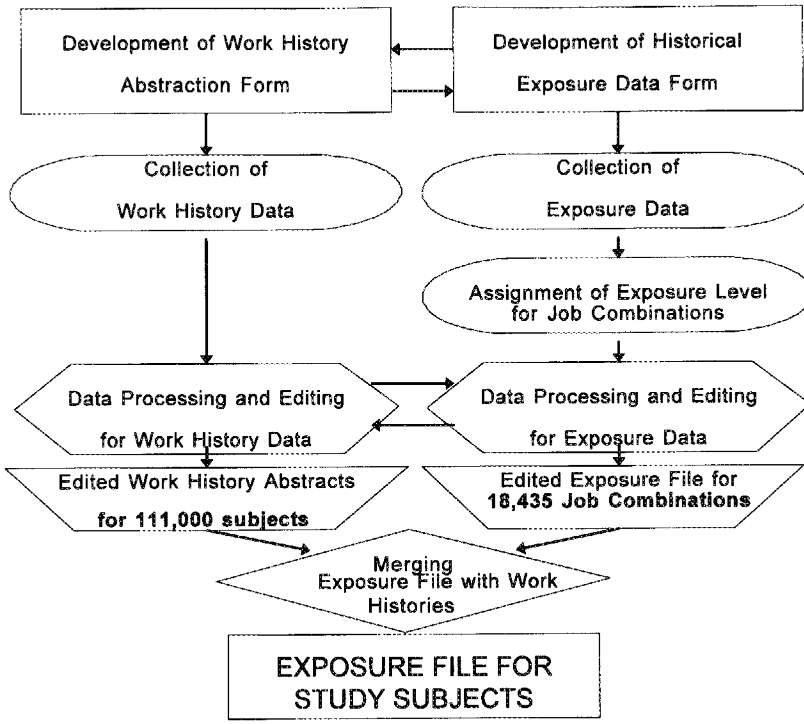

Fig. 1. Steps of exposure assessment procedures used in a cohort study among workers exposed to benzene in China: 1972–1987.

combinations. Under the direction of the principal investigators at IOM-CAPM and National Cancer Institute (NCI), the field center directors and other senior collaborating occupational health personnel from each of the 12 field centers (Shanghai, Tianjin, Chengdu, Chongqing, Harbin, Shenyang, Jinzhou, Zhengzhou, Luoyang, Guangzhou, Nanchang, and Kaifeng) supervised all data collection activities. Exposure data from factories and work history information for study subjects were collected by 370 abstractors in the 12 cities. Assistance in data collection activities was also provided by the work unit supervisors, industrial hygienists, safety officers, and long-term employees in the study factories.

Procedures Used in the Retrospective Exposure Assessment Method

The several steps involved in the exposure assessment are shown in Figure 1. Procedures used in the assessment are summarized below:

I. Development of exposure data forms

Job title dictionary. First, a standardized job title dictionary was developed in which the large number of job titles of workers in Chinese benzene-producing or -using factories was classified into 60 benzene exposure-specific job title categories in 11 major activity groups. A sample of job titles and major activity groups from the dictionary is presented in Table I. The job title dictionary listed each job title by name

TABLE I. Cohort Study of Benzene Workers in China 1972–1987: Sample of Job Titles From Job Title Dictionary

Major activity group	Job titles
1. Paint worker	*Painter *Paint mixer etc.
2. Shoe maker	*Sole gluer *Shoe polisher etc.
3. Insulation worker	*Varnish machine operator *Immersion tank operator etc.
4. Rubber worker	*Rubber cement applicator *Pressing machine operator etc.
5. Chemical worker	*Organic synthesizer *Pesticide production worker etc.
6. Printing worker	*Printing machine operator *Type setter etc.
7. General worker	*Maintenance man *Cleaner, porter etc.

and by study-specific three-digit job title code, and included descriptions of duties related to that job.

Exposure information. Next, exposure information was collected at the factory and the job title level using three various forms.

For control factories with no benzene exposure, information was abstracted at the factory level (nonexposed factory form), including year of first operation, industry classification, the types of raw materials used, and major products made at the factory.

Another form (exposed factory form) was used to collect factory-level exposure information in factories where benzene was used, including industrial classification; major production activities; the types, amounts, and historical changes in benzene-containing raw materials and final products; engineering controls; and use of personal protective equipment. In addition, all study work unit/job title combinations in the factory were identified, all historical measurements for benzene and other organic solvents (e.g., toluene, xylene) recorded, and supplemental information on air monitoring also noted (including the sampling date and sampling location, the associated work unit and job title, and the type of the analytical method used, e.g., gas chromatographic or colorimetric). There were 8,477 benzene measurements available since the 1950s.

A third form (exposed job title form) was used to abstract historical exposure information for seven time periods at the job title level. Field center staff were also required to provide a summary estimate of benzene exposure for each factory/work unit/job title/calendar-year time period combination. As shown in Figure 2, the information on the monitoring data for benzene and other organic solvents, amount of benzene-containing materials used, percent of benzene in materials used (1 = 1–29%; 2 = 30–59%; 3 = 60–100%), average daily frequency of benzene exposure (1 = full time, 2 = half time, 3 = less than 2 hours, or 4 = occasional), historical changes in engineering controls (e.g., general ventilation, local ventilation, closed

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BENZENE COHORT STUDY - FORM 2 - JOB TITLE FORM FOR EXPOSED FACTORY

Factory ID Number: SHANGHAI BICYCLE FACTORY .... |0|1|-|0|0|6| (CITY, FACTORY) — COLUMNS 1-5

1. Job Title: SPRAY PAINTER .... |1|0|1| — 6-8

2. Work Unit: No: 2 .... |0|2| — 9-10

3. Benzene Exposure Table for Job Title — BEGIN CARD |0|6| — 11-12

SUBCARD	01	02	03	04	05	06	07	COLUMNS
	Years							13-14
Parameters	49-59	60-64	65-69	70-74	75-79	80-84	85-Present	
1.1 Type of Measurement	|9|	|9|	|1|	|1|	|9|	|1|	|1|	16
1.2 Average Value of Benzene Concentration (mg/m^3)	|9|9|9|9|	|9|9|9|9|	|0|3|3|1|	|0|1|2|0|	|9|9|9|9|	|0|0|7|2|	|0|0|6|5|	17-20
*2. Existence of Other Chemical Measurements	X 2 3 4 5 6 7 8 9	0X 2 3 4 5 6 7 8 9	X 2 3 4 5 6 7 8 9	X 2 3 4 5 6 7 8 9	X 2 3 4 5 6 7 8 9	0 XX 4 5 6 7 8 9	0 X X 4 5 6 7 8 9	21-29
3.1 Unit Amount of Benzene (1 = Kg; 2 = ton)	|2|	|2|	|2|	|2|	|2|	|2|	|2|	30
3.2 Amount of Benzene Containing Solvent Used per year	|0|1|0|0|	|0|1|0|0|	|0|1|0|0|	|0|2|0|0|	|0|2|0|0|	|0|2|0|0|	|0|2|0|0|	31-34
4. Category of % of Benzene in Solvent	|3|	|3|	|3|	|2|	|2|	|1|	|1|	35
5. Frequency of Exposure 1 = occasional; 2 = < 1/4 day; 3 = half day; 4 = full day	|4|	|4|	|4|	|4|	|4|	|4|	|4|	36
*6. Engineering Control	X 1 2 3 4 5 9	0 X 2 3 4 5 9	0 X 2 3 4 5 9	0 X 2 3 4 5 9	0X 2 3 4 5 9	0 XX 3 4 5 9	0 X X 3 4 5 9	37-43
*7. Personal Protective Equipment	X 1 2 3 4 9	0 X X 3 4 9	0 X X 3 X 9	0 X X 3 X 9	0X X 3X 9	0X X 3X 9	0 XX 3 X 9	44-49
*8. Other Controls	0 1 XX 9	0 1 XX 9	0 XXX 9	0 XXX 9	0XXX 9	0XXX 9	0XXXX 9	50-54
9. Best Exposure Estimate	|0|3|	|0|3|	|0|3|	|2|B|	|2|B|	|2|A|	|2|A|	55-56
*10. Source of Information for Estimates	0 1 2 XX X 6 7 8 9	0 1 2 XX X 6XX 9	0 X 2 XX XXXX 9	0 X 2XXX XXXX 9	0 1 2 XX XXXX 9	0X 2 XX XXXX 9	0X 2 XX XXXX 9	57-66
11. Confidence	|2|	|2|	|1|	|1|	|2|	|1|	|1|	67

Fig. 2. Exposure data form for city/factory/work unit/job title combination in survey of benzene exposed workers in China: 1972–1987.

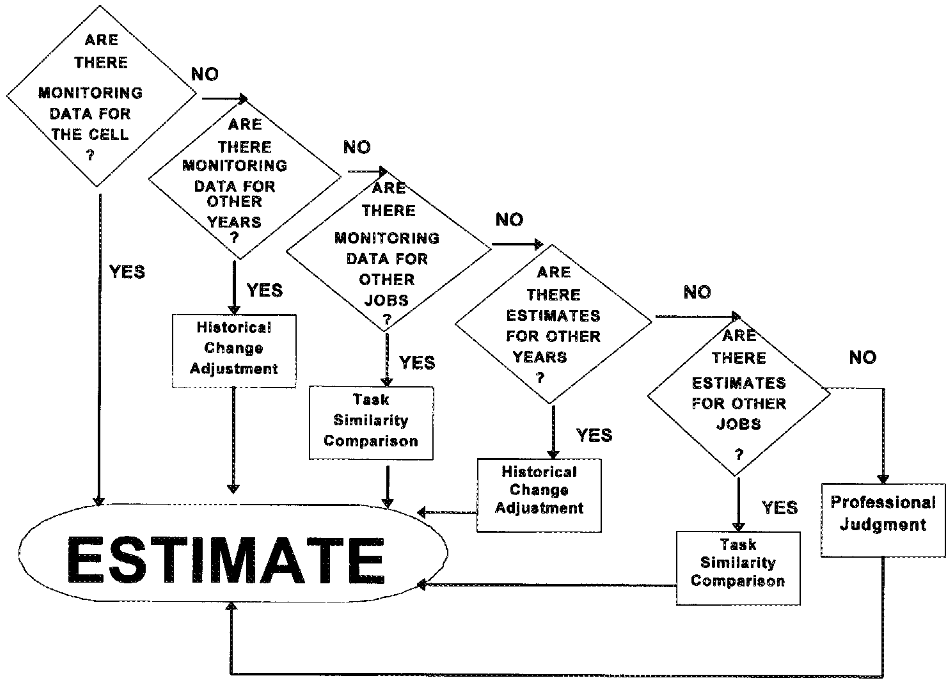

Fig. 3. Strategies for estimating exposure to benzene in a cohort study among workers exposed to benzene in China: 1972–1987.

system, change in the process, or new location), use of personal protective equipment (e.g., gloves, cartridge mask, and/or clothing), and occurrence or change in other control measures (workers' education, environmental monitoring, and physical examination) were recorded on the form. The estimate of benzene exposure level was carried out by local industrial hygienists and other occupational health personnel for each work unit/job title/calendar period combination in six concentration ranges (00 = <1 parts per million [ppm]; 1A = 1–5 ppm; 1B = 6–10 ppm; 2A = 11–25 ppm; 2B = 26–50 ppm; and 03 = >50 ppm), using the assignment strategy described below (Section II). Finally, the source of information used to make the benzene exposure estimate (such as air level measurements, control measures, or professional judgment) and the assigner's confidence in the estimate (very confident, confident, and not confident) were recorded on the form.

II. Assignment of exposure levels

As shown in Figure 3, if there were benzene monitoring data which were consistent with the other exposure information, then the estimate was derived from the mean of the measurements adjusted for the frequency of exposure to benzene (Item 5 on Fig. 2). If there was no monitoring information for the specific work unit/job title/calendar period or if the measurement results were not consistent with the other exposure information, then monitoring data for the same work unit/job combination in other calendar periods were used, after adjustments for historical changes and exposure frequency, or if there were no monitoring data for the specific

TABLE II. Cohort Study of Benzene Workers in China 1972–1987: Distribution of Exposure Variables and Estimates Over Seven Calendar-Year Periods

Exposure parameters	1949–1959	1960–1964	1965–1969	1970–1974	1975–1979	1980–1984	85+	All years
No. of estimates made	1,522	2,041	2,581	2,914	3,095	3,159	3,123	18,435
No. of measurements done	44	256	386	457	1,766	2,551	2,950	8,477
No. of estimates based on meas.	52	217	326	591	1,643	1,956	2,111	6,896
% estimates based on measurements	3.4	10.6	12.6	20.3	53.1	61.9	67.6	37.4
Mean of measurements (ppm)	25	33	33	27	15	11	8	13
% benzene in materials	40	41	40	36	32	30	28	34
Duration of exposure/day (hours)	4.3	4.3	3.8	4.1	4.3	4.3	4.3	4.2
% jobs having general ventilation	63	68	75	77	81	85	86	78
% jobs having local ventilation	39	44	52	58	64	77	81	62
% jobs having closed system	2	2	4	5	7	11	13	7
% jobs having process change	2	4	7	10	18	36	46	20
% jobs having glove	87	92	93	94	96	98	98	95
% jobs having cloth mask	87	91	92	93	95	97	97	94
% jobs having cartridge mask	5	11	12	16	24	30	31	20
% jobs having work clothing	83	86	87	89	92	93	93	90
% jobs having monitoring	7	22	27	40	81	94	98	59
% jobs having safety education	37	47	52	61	77	91	93	69
% jobs having physical exam	15	25	27	44	83	98	99	62
Mean of estimates (ppm)	20.4	19.6	17.5	17.2	16.8	13.9	11.5	16.7
% estimates with high confidence	2	6	6	11	31	38	42	22

job combination in any calendar period, monitoring results for similar job combinations were used after task description comparisons and historical changes were considered. If none of the above sources were available, the field center staff used all available exposure information and their professional judgment to estimate the exposure.

III. Work histories of study subjects

The individual work history information abstracted from written factory records included the names of study factories, work units (department), and job titles held by the subject, with starting and ending dates of each job. Job title codes were assigned for each individual job based upon the job title dictionaries.

IV. Data editing and processing

Following data collection and exposure assignment, all forms were sent to the data editing and processing center in Beijing. Machine editing, including logic and range checks, was carried out. Data were reviewed to resolve discrepancies if the benzene exposure estimates were not consistent with the exposure information. Discrepancies between the completed work history forms and exposure data collection forms were resolved by further data retrieval from the field centers.

V. Merging work histories with exposure data

Files of subjects' work histories and the exposure data were merged to assign estimated exposure levels for each study subject on the basis of factory/work unit/job title/calendar-year combination. Several exposure indices (e.g., cumulative exposure, average exposure) were developed for each study subject using information on level and duration of exposure for the jobs held by the subject.

TABLE III. Benzene Exposure Estimates (in ppm) for Major Industries Over Seven Calendar-Year Periods in China

Major industry groups	No. of estimates	1949–1959	1960–1964	1965–1969	1970–1974	1975–1979	1980–1984	1985–1987	All years
Food	119	15.0	8.3	7.6	10.2	8.6	8.5	10.7	9.1
Textile	239	17.3	14.8	11.9	14.7	11.4	9.8	11.3	12.6
Leather products	2,237	19.1	21.7	22.7	17.6	15.0	12.7	12.5	16.0
Wood and furniture	854	35.0	39.4	27.2	16.7	14.2	15.2	17.1	22.3
Paper products	79	12.9	12.9	12.9	12.9	12.9	14.6	13.9	13.3
Stationery	560	17.8	19.7	19.6	17.8	14.4	12.9	11.6	16.1
Printing	284	34.7	24.3	28.4	21.6	23.8	21.6	16.9	22.9
Agricultural chemical	262	13.3	12.7	10.8	13.7	22.6	14.5	9.1	14.1
Organic chemical	1,429	18.1	15.3	16.7	19.1	16.5	9.8	7.2	14.3
Other chemical	350	24.5	25.5	8.6	24.9	19.3	17.7	18.2	19.7
Pharmaceutical	98	13.6	12.8	6.8	20.1	13.2	14.7	5.1	12.4
Rubber and plastic	1,205	47.0	38.3	39.3	34.9	33.4	21.1	10.6	30.7
Petroleum products	165	40.3	27.0	17.1	20.8	15.2	12.2	23.3	19.9
Glass products	159	12.4	8.9	6.4	7.9	4.3	2.7	2.1	6.2
Metallurgy	192	19.7	18.0	10.5	13.3	19.9	22.8	17.3	17.3
Fabricated metal	428	33.1	27.0	18.5	20.2	16.5	16.3	16.3	19.4
Machinery	3,247	16.5	16.0	14.8	15.6	15.2	13.9	11.7	14.6
Electrical equipment	3,389	15.0	13.5	10.4	9.9	12.0	9.2	8.2	10.8
Transportation equipment	2,116	16.2	15.6	15.6	17.0	18.3	16.3	11.0	15.7
Precision machinery	445	13.4	14.1	15.3	18.3	18.2	16.5	14.0	16.0
Other manufacturing	282	16.6	25.2	28.0	27.6	21.7	24.6	21.4	23.9
Construction	142	11.2	9.3	10.2	12.1	26.2	24.2	7.6	15.2
Others	154	20.6	18.8	15.0	42.5	36.8	19.9	19.6	24.5
All industries	18,435	20.4	19.6	17.5	17.2	16.8	13.9	11.5	16.7

RESULTS

Distributions of exposure estimates, measurement results, and other exposure variables over the seven calendar-year periods are presented in Table II. There were a total of 18,435 benzene exposure estimates, 38% based on monitoring data, primarily collected after 1975. The measured benzene concentrations ranged from 25–33 ppm prior to 1975, and 8–15 ppm afterward. Although the percentage of benzene in raw materials or products declined from 40 to 28% during the seven calendar-year periods, the average daily duration of exposure (4.2 hours per day) showed little change. Implementation of the control measures either in the factory or particularly in the work unit steadily increased over the years. The summary estimated exposure levels for benzene showed a declining trend over time. On average, over the seven time periods, the estimated benzene exposure level was 16.7 ppm, ranging from 20.4 ppm in the first period to 11.5 ppm in the last period. Percentage of estimates made with high confidence increased over time, from 2% to 42% for the first and last periods, respectively.

Benzene exposure estimates by major industries are presented in Table III. Manufacturing industries characterized by high-level exposure included rubber-plastic, wood-furniture, printing, petroleum products, fabricated metal, and other chemical manufacturing industries, whereas the glass products, electrical equipment, and food processing industries had lower exposure to benzene.

Benzene exposure levels for major occupations are shown in Table IV. Similar

TABLE IV. Benzene Exposure Estimates (in ppm) for Major Occupations Over Seven Calendar-Year Periods in China

Major occupational groups	No. of estimates	1949–1959	1960–1964	1965–1969	1970–1974	1975–1979	1980–1984	1985–1987	All years
Spray painters	3,054	26.8	25.1	22.1	23.5	24.0	20.7	16.5	22.2
Brush painters	1,796	20.9	21.7	17.4	17.0	17.9	15.2	15.5	17.7
Immersion painters	593	17.7	16.0	16.1	17.1	20.7	15.9	16.3	17.1
Electrostatic painters	125	43.7	47.7	27.7	23.0	10.7	9.9	8.3	21.2
Drip painters	86	49.6	51.2	50.7	29.6	25.8	17.0	15.3	32.2
General painters	612	12.0	12.2	11.0	14.8	20.3	18.5	13.9	15.1
Paint mixers	607	27.6	25.0	23.9	22.0	18.7	20.1	17.5	21.7
Paint dryers	239	20.6	17.8	12.6	10.9	11.0	9.9	8.8	12.4
Painter helpers	233	15.8	12.1	12.1	12.5	8.8	8.6	5.0	9.4
Paint makers	539	30.2	25.0	20.9	29.3	28.9	17.6	14.1	23.4
Paint filter workers	55	10.9	7.9	8.1	7.3	7.3	1.5	1.8	6.2
Paint packers	188	32.6	24.6	21.4	26.7	26.5	14.5	13.8	22.3
Upper shoe gluers	276	42.6	36.7	43.4	31.1	19.4	18.1	20.5	26.2
Sole shoe gluers	386	25.4	37.8	35.6	27.8	22.4	19.7	16.1	24.2
Shoe glue mixers	261	32.4	27.4	32.1	27.3	23.2	20.3	18.3	24.3
Shoe polishers	98	22.5	18.3	15.2	12.7	17.3	17.7	29.3	18.9
Shoe pinkers	370	11.8	14.2	14.4	12.0	13.6	11.4	10.6	12.3
Shoe glue grinders	149	15.0	15.1	11.9	9.3	10.7	9.3	13.2	11.3
Shoe finishers	212	10.8	11.1	9.2	9.2	9.3	8.6	7.9	9.0
Varnishers	114	27.2	20.2	18.2	19.2	12.1	9.9	9.4	16.2
Varnish mixers	83	21.4	21.7	20.2	24.9	14.9	7.3	7.9	16.1
Varnish checkers	56	12.1	12.1	12.1	9.9	9.9	6.1	6.7	9.9
Rubber glue applicators	204	66.0	57.0	68.2	55.1	57.9	48.2	26.1	52.6
Rubber rolling workers	39	56.0	32.6	32.6	32.6	32.6	29.7	11.4	31.8
Rubber vulcanizers	134	53.7	49.5	58.3	47.0	38.2	30.4	18.3	40.8
Rubber modelling workers	181	68.9	63.0	64.8	62.8	65.9	30.4	11.8	51.6
Rubber mixing workers	39	64.0	51.7	51.7	51.7	45.6	25.8	6.0	39.2
Rubber material workers	40	32.5	11.0	38.2	37.5	11.6	6.7	3.0	18.9
Organic chemical workers	114	46.9	43.9	48.1	57.5	41.7	26.3	18.4	37.9
Insecticide production workers	68	28.7	33.1	23.8	35.7	33.8	24.5	18.3	28.4
Benzene production workers	49	17.4	25.0	12.2	28.0	22.3	25.0	43.7	26.4
Pharmaceutical workers	40	18.6	17.9	4.8	27.8	15.3	17.5	10.9	16.1
Benzene extractor workers	10	n/a	2.2	2.2	8.6	8.6	8.6	1.3	5.9
Printing workers	253	26.3	21.8	16.8	18.9	22.6	21.0	15.6	19.8
Other benzene workers	633	25.8	23.5	21.3	24.0	23.7	22.2	17.4	22.2
General helpers	976	15.2	16.2	12.3	9.4	7.6	6.1	4.3	9.4
Maintenance workers	732	13.5	13.8	12.2	11.5	11.1	9.5	8.2	11.1
Supervisors, foreman	2,119	6.3	5.8	4.9	4.9	4.6	4.0	3.3	4.6
Engineers, technicians	1,158	6.9	7.8	7.1	5.1	5.4	4.7	3.4	5.6
Cleaners, janitors	116	8.2	7.1	7.4	5.4	3.3	4.1	3.8	5.2
Porters, material movers	230	15.3	13.4	8.3	7.0	6.8	6.2	2.7	7.8
Warehouse workers	728	7.1	7.0	5.5	7.3	4.8	4.5	3.6	5.5
Nonspecific jobs	440	7.2	6.3	6.0	4.3	4.0	3.7	3.2	4.9
All occupations	18,435	20.4	19.6	17.5	17.2	16.8	13.9	11.5	16.7

to findings for major industries, the highest benzene exposure was observed among rubber workers, especially among rubber glue applicators with an average estimated exposure level of 52.6 ppm. Painters (spray, electrostatic, drip painters, and paint mixers), paint manufacturing workers, shoe glue applicators, and chemical manufacturing workers (organic, insecticide, and benzene production workers) were also highly exposed (average level greater than 20 ppm).

DISCUSSION

Although benzene is a recognized leukemogen, many aspects of the benzene-leukemia dose-response relationship require additional clarification [IARC, 1987]. It is also not clear whether benzene can cause other types of cancer. The cohort study among workers exposed to benzene in 672 factories in 12 Chinese field centers was initiated to investigate these issues. The large size of the study required the development and implementation of a systematic exposure assessment methodology as described herein.

The accuracy of exposure estimates is dependent on the availability and type of historical exposure data. There are several advantages in carrying out occupational epidemiologic investigations in the People's Republic of China, including large numbers of study subjects, fewer jobs held per subject, fewer exposures per subject, easier access to factory records, and administrative systems for tracing and follow-up. The average number of jobs held by a subject in the present study was 1.4, in contrast with 5–10 in most occupational studies in the United States [Stewart et al., 1986]. Because Chinese workers hold fewer jobs and generally have fewer types of exposures in industrial jobs than workers in western industrialized countries, the potential for confounding by other hazardous substances is reduced.

A limitation of the approach used in this study was the inability of the central team of industrial hygienists to walk through all of the 672 study factories. Nevertheless, a standardized approach was developed and intensive training undertaken to utilize the experience of the individual factory industrial hygienists and safety officers. A benzene exposure-specific job title dictionary was developed for all benzene-related jobs so that job title codes would be uniformly assigned. Although the dictionary included fewer jobs than other existing occupational coding systems, the job titles in the benzene study dictionary were specific to benzene exposure. This level of detail would not have been possible if a standard job title classification system had been used. Another limitation was the lack of personal sampling for air monitoring. Virtually all of the benzene measurements were based on short-term area sampling.

Although multicenter decision making may lead to differences in interpretation of the historical exposure information, every effort was made to standardize the assignment of exposure, including central training of the field center directors and central editing procedures carried out at the IOM-CAPM and at NCI. Because of these limitations and the historical nature of the retrospective exposure assessment, exposure ranges were used rather than quantitative point estimates.

In summary, the retrospective exposure assessment method described in this report evolved from a challenging effort to estimate exposure to benzene in a large scale, multicenter, multi-industry cohort mortality study, using all available historical exposure information. Although the assessment approach was developed for a specific study, we believe that it will be a useful tool for other multicenter investigations of benzene and other types of exposures.

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